Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1644PNH

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 6	Mar 08	Gene Names now available in BIOSIS
NEWS 7	Mar 22	TOXLIT no longer available
NEWS 8	Mar 22	TRCTHERMO no longer available
NEWS 9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
NEWS 11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS 12	Apr 08	"Ask CAS" for self-help around the clock
NEWS 13	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 14	Apr 09	ZDB will be removed from STN
NEWS 15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 18	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 19	Jun 03	New e-mail delivery for search results now available
NEWS 20	Jun 10	MEDLINE Reload
NEWS 21	Jun 10	PCTFULL has been reloaded

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:57:15 ON 02 JUL 2002

```
=> file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 11:57:43 ON 02 JUL 2002

FILE 'EMBASE' ENTERED AT 11:57:43 ON 02 JUL 2002
COPYRIGHT (C) 2002 Elsevier Science B.V.  All rights reserved.

FILE 'BIOSIS' ENTERED AT 11:57:43 ON 02 JUL 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'SCISEARCH' ENTERED AT 11:57:43 ON 02 JUL 2002
COPYRIGHT (C) 2002 Institute for Scientific Information (ISI) (R)

FILE 'CAPLUS' ENTERED AT 11:57:43 ON 02 JUL 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> s lymph node immunization
L1          104 LYMPH NODE IMMUNIZATION

=> s l1 adn allergy
MISSING OPERATOR L1 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l1 and allergy
L2            1 L1 AND ALLERGY

=> d l2 cbib abs

L2   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
1976:15580   Document No. 84:15580  Control of immune response.  I.  Depression
     of DNA synthesis by immune lymph node cells.  Asherson, G. L.; Wood, P.
     J.; Mayhew, Barbara (Div. Immunol., Clin. Res. Cent., Harrow, Engl.).
     Immunology, 29(6), 1057-65 (English) 1975.  CODEN: IMMUAM.
AB   After immunization of mice with picryl chloride the DNA response in the
     regional lymph nodes draining the site of immunization reached a peak on
     day 3 after immunization and fell to preimmunization levels by day 6.
     Prior i.v. injection with 40 .times. 106 immune lymph node cells depressed
     the day 4 DNA response by .apprx.60% but injection with 0.3 .times. 106
     cells increased the DNA response.  Similar results were obtained with
     another contact sensitizing agent, oxazolone, but cells immunized with
     oxazolone did not affect the DNA response to picryl chloride.


=> s l1 ad axillary
MISSING OPERATOR L1 AD
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l1 and axillary lymph node
L3            0 L1 AND AXILLARY LYMPH NODE

=> s l1 adn inguinal
MISSING OPERATOR L1 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.
```

```
=> s l1 and inguinal
L4            4 L1 AND INGUINAL

=> dup remove l4
PROCESSING COMPLETED FOR L4
L5            1 DUP REMOVE L4 (3 DUPLICATES REMOVED)

=> d l5 cbib abs

L5   ANSWER 1 OF 1     MEDLINE                                DUPLICATE 1
89292707  Document Number: 89292707.     PubMed ID: 2661691.   The production of
      polyclonal and monoclonal antibodies in mice using novel immunization
      methods. Hong T H; Chen S T; Tang T K; Wang S C; Chang T H. (Cell Biology
      and Immunology Division, Development Center for Biotechnology, Taipei,
      Taiwan. ) JOURNAL OF IMMUNOLOGICAL METHODS, (1989 Jun 21) 120 (2) 151-7.
      Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands.
      Language: English.
AB    Two novel immunization methods (intrasplenic and intra-inguinal
      lymph node) have been developed for the production of polyclonal and
      monoclonal antibodies in mice. Freund's complete adjuvant and antigen were
      mixed in the ratio of 1:2 (v/v). Various concentrations of human serum
      albumin (HSA) were used as antigen. No primary immune response was induced
      with 0.1 microgram of HSA in either of the methods studied. Intrasplenic
      immunization resulted in the strongest primary immune responses using all
      other doses of HSA. The primary immune response induced by intrasplenic
      immunization with 0.5 microgram of HSA was higher than any response
      induced by subcutaneous immunization with various doses of HSA.
      Inguinal lymph node immunization was
      less effective than intrasplenic immunization but better than subcutaneous
      immunization with 1-50 micrograms of HSA. Comparisons were also made of
      the efficacy of different adjuvants when inducing primary immune responses
      with 1 microgram of HSA. Freund's complete adjuvant resulted in a much
      stronger response than Freund's incomplete adjuvant and alum. Both
      intrasplenic and inguinal lymph node
      immunization using 1-5 micrograms of HSA were able to induce
      strong primary immune responses. Secondary immunization with either method
      or intravenous injection 3 days before fusion resulted in a higher
      frequency of specific monoclonal antibodies.


=> s l1 and bee venom
L6            0 L1 AND BEE VENOM

=> s l1 and allergen
L7            0 L1 AND ALLERGEN

=> s l1 and radiological method
L8            0 L1 AND RADIOLOGICAL METHOD

=> d his

     (FILE 'HOME' ENTERED AT 11:57:15 ON 02 JUL 2002)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 11:57:43 ON
     02 JUL 2002
L1          104 S LYMPH NODE IMMUNIZATION
L2            1 S L1 AND ALLERGY
L3            0 S L1 AND AXILLARY LYMPH NODE
L4            4 S L1 AND INGUINAL
L5            1 DUP REMOVE L4 (3 DUPLICATES REMOVED)
L6            0 S L1 AND BEE VENOM
L7            0 S L1 AND ALLERGEN
L8            0 S L1 AND RADIOLOGICAL METHOD
```

=> s l1 and injection
L9 16 L1 AND INJECTION

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10 10 DUP REMOVE L9 (6 DUPLICATES REMOVED)

=> d l10 1-10 cbib abs

L10 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2002 ACS
2001:790358 Document No. 136:68365 Immunization with the adjuvant MF59 induces macrophage trafficking and apoptosis. Dupuis, Marc; Denis-Mize, Kimberly; LaBarbara, Allyson; Peters, Wendy; Charo, Israel F.; McDonald, Donald M.; Ott, Gary (Cardiovascular Research Institute and Department of Anatomy, University of California, San Francisco, CA, USA). European Journal of Immunology, 31(10), 2910-2918 (English) 2001. CODEN: EJIMAF. ISSN: 0014-2980. Publisher: Wiley-VCH Verlag GmbH.
AB The mechanisms assocd. with the immunostimulatory activity of vaccine adjuvants are still poorly understood. The authors have undertaken a study to det. whether antigen-presenting cell trafficking is modified by administration of the submicron emulsion adjuvant MF59. The authors investigated the fate of inflammatory macrophages after i.m. **injection** of the antigen herpes simplex virus gD2 with fluorescence-labeled MF59. A homogenous population of macrophages infiltrated the muscle, internalized adjuvant and expressed markers characteristic of mature macrophages over a 48-h period. Macrophage influx to the **injection** site was reduced by 70% in mice deficient for the chemokine receptor 2 (CCR2). Two distinct cell populations were shown to contain fluorescence-labeled MF59 in the draining lymph node at 48 h post **injection**. The first population had a round morphol., exhibited bright fluorescence, was located in the subcapsular sinus, and was apoptotic. The second population had a dendritic morphol., was weakly fluorescent, and was located in the T cell area where adjuvant-contg. apoptotic bodies identified by TUNEL labeling were present. The authors propose that lymph node-resident dendritic cells can acquire antigen and MF59 after i.m. immunization by uptake of the apoptotic macrophages.

L10 ANSWER 2 OF 10 MEDLINE
2001522716 Document Number: 21454062. PubMed ID: 11567745. Targeted **lymph node immunization** can protect cats from a mucosal challenge with feline immunodeficiency virus. Finerty S; Stokes C R; Gruffydd-Jones T J; Hillman T J; Barr F J; Harbour D A. (Department of Clinical Veterinary Science, University of Bristol, Langford, BS40 5DU, Bristol, UK.. sue.finesrty@bristol.ac.uk) . VACCINE, (2001 Oct 12) 20 (1-2) 49-58. Journal code: 8406899. ISSN: 0264-410X. Pub. country: England: United Kingdom. Language: English.
AB With the rapid spread of human immunodeficiency virus (HIV) infection worldwide it is clear that effective strategies for mucosal vaccination against lentiviruses are urgently required. The aim of the present study is to determine whether protective immune responses against a mucosal challenge by feline immunodeficiency virus (FIV) can be elicited by targeting the immunization to the medial iliac lymph nodes--the principal site of migration of cells from the genital and rectal mucosa. Cats were challenged with homologous FIV via the rectal route. Targeted **lymph node immunization** was found to be an effective route of immunization eliciting both humoral and proliferative responses to peptide-based and fixed cell vaccines. Vaccination with fixed virus infected cells elicited protection against a cell-free mucosal FIV challenge. In addition, some cats vaccinated with fixed uninfected cells also remained uninfected following a cell-associated FIV challenge.

L10 ANSWER 3 OF 10 SCISEARCH COPYRIGHT 2002 ISI (R)
1999:835302 The Genuine Article (R) Number: 249QD. Targeted salivary gland immunization with plasmid DNA elicits specific salivary immunoglobulin A and G antibodies and serum immunoglobulin G antibodies in mice. Kawabata S (Reprint); Terao Y; Fujiwara T; Nakagawa I; Hamada S. OSAKA UNIV, FAC DENT, DEPT ORAL MICROBIOL, 1-8 YAMADAOKA, SUITA, OSAKA 5650871, JAPAN (Reprint); OSAKA UNIV, FAC DENT, DEPT PEDODONT, SUITA, OSAKA 5650871, JAPAN. INFECTION AND IMMUNITY (NOV 1999) Vol. 67, No. 11, pp. 5863-5868. Publisher: AMER SOC MICROBIOLOGY. 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171. ISSN: 0019-9567. Pub. country: JAPAN. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB For the development of vaccines against oral and pharyngeal pathogens invading the mucosal epithelia, both secretory and serum immunoglobulin A (IgA) and IgG antibodies and cytotoxic T lymphocytes (CTL) have been induced. We used a novel approach, targeted salivary gland (TSG) immunization, using plasmid pcDNA3/fimA, coding for Porphyromonas gingivalis fimbriae, Expression of subunit protein, fimbrillin, was observed in eukaryotic cells growing in vitro following transfection with pcDNA3/fimA, In this study, we obtained good humoral and cell-mediated immune responses in BALB/c mice by TSG administration using the above-mentioned DNA vaccine. The production of fimbria-specific IgA and IgG antibodies in saliva and serum IgG antibody was significantly stimulated by TSG immunization. **Injection** of DNA vaccine into salivary gland elicited high-level production of antigen-specific IgG antibody, similar to that induced following intramuscular immunization. The major IgG subclass that recognized fimbriae was IgG2a in serum from pcDNA3/fimA-immunized mice. Reverse transcription-PCR analysis of mononuclear cells from salivary glands showed that levels of Th2 cytokine-specific mRNA were higher in the immunized group than in the nonimmunized group. In addition, TSG DNA immunization resulted in the generation of antigen-specific CTL in spleen. These results indicate that TSG immunization with plasmid DNA may represent a genetic immunization strategy against infection by oral and pharyngeal pathogens that may invade local, mucosal surfaces.

L10 ANSWER 4 OF 10 SCISEARCH COPYRIGHT 2002 ISI (R)
1999:224190 The Genuine Article (R) Number: 175YD. Comparison between targeted and untargeted systemic immunizations with adjuvanted urease to cure Helicobacter pylori infection in mice. Guy B (Reprint); Hessler C; Fourage S; Rokbi B; Millet M J Q. PASTEUR MERIEUX CONNAUGHT, RES DEPT, F-69280 MARCY LETOILE, FRANCE (Reprint). VACCINE (5 MAR 1999) Vol. 17, No. 9-10, pp. 1130-1135. Publisher: ELSEVIER SCI LTD. THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND. ISSN: 0264-410X. Pub. country: FRANCE. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Outbred OF1 mice infected in a first step with a mouse-adapted Helicobacter pylori strain were immunized in a second step by systemic or mucosal routes: systemic immunizations were performed subcutaneously with adjuvanted urease either in the infra or supra-diaphragmatic region of the body, while mucosal immunization was done with urease in the presence of E. coil heat Labile toxin. Mucosal and subcutaneous immunizations induced in infected mice a significant reduction in bacterial density whatever the site of **injection** but complete eradication was preferentially observed in mice immunized subcutaneously in the back. Systemic immunization with appropriate schedules and formulations could constitute a valuable approach to cure Helicobacter pylori infection.

L10 ANSWER 5 OF 10 MEDLINE DUPLICATE 1
95138334 Document Number: 95138334. PubMed ID: 7836584. Effect of whole Staphylococcus aureus and mode of immunization on bovine opsonizing antibodies to capsule. Guidry A J; O'Brien C N; Oliver S P; Dowlen H H;

Douglass L W. (Milk Secretion and Mastitis Laboratory, Agricultural Research Service, Beltsville, MD 20705.) JOURNAL OF DAIRY SCIENCE, (1994 Oct) 77 (10) 2965-74. Journal code: 2985126R. ISSN: 0022-0302. Pub. country: United States. Language: English.

AB Exopolysaccharide capsule is a major virulence factor of Staphylococcus aureus because it inhibits neutrophil recognition of antibodies to highly antigenic S. aureus cell wall. To circumvent this inhibition, two modes of immunization were tested for ability to induce anticapsular opsonins. Cows were immunized at drying off and boosted on d 14 and 28 by **injection** of Smith diffuse S. aureus plus dextran sulfate in the area of the supramammary lymph node or intramammarily. In cows immunized in the area of the supramammary lymph node, IgG1 and IgG2 sera antibody titers to capsule increased and remained elevated to the end of the study, 120 d postcalving. The IgM titers increased during the dry period but declined to preimmunization levels at calving. Response of serum IgG1 and IgM to intramammary immunization was similar to that with supramammary **lymph node immunization**, but more delayed and lower in magnitude. Antibodies of all four isotypes, IgG1, IgG2, IgA, and IgM, increased in dry secretions following immunization via lymph node. In cows immunized in the lymph node, IgG1 antibodies remained elevated throughout the study, but IgG2 antibodies dropped to baseline 15 d postcalving. In cows immunized intramammarily, only IgA antibodies increased significantly in lacteal secretions and remained elevated throughout the study. Immunization of cows in the lymph node during the dry period enhanced the ability of dry secretions and colostrum to support phagocytosis.

L10 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2002 ACS

1994:214656 Document No. 120:214656 High titer anti-cytokine antibodies obtained by intra-**lymph node immunization** with low amounts of antigen. Coupey, Lionel; Berrada, Lamya; Gascan, Hughes; Godard, Anne; Praloran, Vincent (Lab. Hematol. Exp., Fac. Med., Limoges, 87 025, Fr.). Cytokine (Philadelphia), 5(6), 564-9 (English) 1993. CODEN: CYTIE9. ISSN: 1043-4666.

AB Intra-**lymph node immunization** was performed on rabbits to obtain anti-cytokine antibodies using low or very low amts. of the following purified cytokines: CSF-1 (or M-CSF: 10, 2 or 0.2 .mu.g/ **injection**), GM-CSF (10 .mu.g/**injection**), IL-2 (10 .mu.g/ **injection**) and HILDA/LIF (10 .mu.g for the first **injection** and 5 .mu.g/**injection** for boosts). This technique is easily performed by dissection of the popliteal lymph node. Specific high titer antibodies were obtained after the first or second boost for antigen doses between 10 (for all cytokines tested) and 0.2 .mu.g (for CSF-1) per **injection**. In most cases, these antibodies could be used for immunopptn., competition assays, dot immunoblotting, neutralization of biol. activity and receptor binding inhibition. Some applications show that these tools are useful for cytokine research projects. For newly identified cytokines available in limited amts., this method of obtaining specific polyclonal antibodies is an interesting alternative to the expensive, time-consuming and tech. more demanding monoclonal antibody method.

L10 ANSWER 7 OF 10 MEDLINE DUPLICATE 2

89292707 Document Number: 89292707. PubMed ID: 2661691. The production of polyclonal and monoclonal antibodies in mice using novel immunization methods. Hong T H; Chen S T; Tang T K; Wang S C; Chang T H. (Cell Biology and Immunology Division, Development Center for Biotechnology, Taipei, Taiwan.) JOURNAL OF IMMUNOLOGICAL METHODS, (1989 Jun 21) 120 (2) 151-7. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB Two novel immunization methods (intrasplenic and intra-inguinal lymph node) have been developed for the production of polyclonal and monoclonal antibodies in mice. Freund's complete adjuvant and antigen were mixed in

the ratio of 1:2 (v/v). Various concentrations of human serum albumin (HSA) were used as antigen. No primary immune response was induced with 0.1 microgram of HSA in either of the methods studied. Intrasplenic immunization resulted in the strongest primary immune responses using all other doses of HSA. The primary immune response induced by intrasplenic immunization with 0.5 microgram of HSA was higher than any response induced by subcutaneous immunization with various doses of HSA. Inguinal **lymph node immunization** was less effective
than intrasplenic immunization but better than subcutaneous immunization with 1-50 micrograms of HSA. Comparisons were also made of the efficacy of different adjuvants when inducing primary immune responses with 1 microgram of HSA. Freund's complete adjuvant resulted in a much stronger response than Freund's incomplete adjuvant and alum. Both intrasplenic and inguinal **lymph node immunization** using 1-5
micrograms of HSA were able to induce strong primary immune responses. Secondary immunization with either method or intravenous **injection**
3 days before fusion resulted in a higher frequency of specific monoclonal antibodies.

L10 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1982:238930 Document No.: BA74:11410. TUMOR SPONGE IMPLANTATION AN IN-VIVO METHOD FOR STUDYING SYNGENEIC PRIMARY ANTI TUMOR LYMPHOCYTE RESPONSES. VALLERA D A; MENTZER S J; MAIZEL S E. DEP. THERAPEUTIC RADIOL., BOX 367, MAYO MEML. BUILDING, UNIV. MINN., MINNEAPOLIS, MINN. 55455.. CANCER RES, (1982) 42 (2), 397-404. CODEN: CNREA8. ISSN: 0008-5472. Language: English.
AB Sponge matrices surgically implanted in the s.c. space of the back of normal BALB/c mice were injected with a regressor dose of Moloney sarcoma virus-induced BALB/c tumor cells [MSV-124]. The kinetics of the generation of cytotoxic cells within the sponge was studied over a 22-day period in a short-term 51Cr release assay. Cytotoxic activity peaked on day 16 and then declined to negligible levels by day 22. No cytotoxicity was detectable when nontransformed BALB/c blast cells, Moloney leukemia virus-induced tumor (LSTRA) cells or unrelated chemically induced tumor (EL4) cells were used as targets. When the cellular composition of implanted tumor sponges was examined on day 16, it was 30-40% myeloperoxidase-positive cells, 15-25% surface Ig-positive cells and 40-50 .theta.-positive cells. Treatment with anti-Thy 1.2 plus complement eliminated the cytotoxic response on day 16. The ratio of T-cells to tumor cells within the sponge was determined by immunofluorescence. Kinetic studies showed that the number of .theta.-positive cells increased well before cytolytic activity was detected, possibly reflecting increasing numbers of amplifier T-cells or cytotoxic cell precursors. A later decline in .theta.-positive cells correlated directly with decreased cytotoxicity. Furthermore, onset of cytotoxic activity also correlated with a decline in the percentage of Moloney murine sarcoma virus tumor cells within the sponge. Sponge cells isolated on day 16 (peak cytotoxicity), mixed with lethal dosages of Moloney murine sarcoma virus tumor cells, successfully neutralized the lethal challenge demonstrating the in vivo antitumor efficacy of these effector cells. Sponges were also implanted in mice which had been immunized with a single **injection** of Moloney
murine sarcoma virus cells. Inoculation of the sponge with tumor cells resulted in a 2nd set response in which cytotoxic cells appeared much earlier than in unsensitized animals. Cells from spleen, lymph node or peritoneal cavity of normal or presensitized animals with tumor sponge implants were not cytotoxic, suggesting a highly localized response.

L10 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2002 ACS
1978:404479 Document No. 89:4479 Antigen modulation of the immune response. V. Generation of large memory cells in antigen draining lymph nodes. Feldbush, Thomas L.; Stewart, Nancy (Dep. Microbiol. Urol., Univ. Iowa, Iowa City, Iowa, USA). Cell. Immunol., 37(2), 336-48 (English) 1978. CODEN: CLIMB8. ISSN: 0008-8749.
AB When the nonantigen-draining mesenteric lymph nodes were examd. 4 wk after

i.p. immunization with dinitrophenylated bovine .gamma.-globulin (DNP-BGG), large memory B cells were present in only very low nos. However, when the draining parathymic nodes were removed, a significant enrichment of large memory cell activity was seen. When the results were cor. for the cell yields in each 1g sepd. fraction, 59% of the total memory cells were small, 36% medium, and 5% large in the mesenteric lymph node prepns. and 40% were small, 46% medium, and 14% large in the parathymic lymph node suspensions. When popliteal lymph nodes were removed after footpad immunization, 32% of the total memory cell activity was in the small cell fraction while 49% was in the medium fraction and 18% in the large cell fraction. Control expts. were also run to show that the shift in the velocity sedimentation profile of the various memory cell populations was not an artifact of the adoptive transfer system nor a result of selective antigen triggering. Apparently, the size distribution of memory cells depends upon the source of cells studied, large memory cells being found predominantly only in lymph nodes draining the site of antigen **injection**. Since the large memory cells can also be found in the thoracic duct lymph after footpad immunization but not after i.p. immunization, it is suggested that the larger cells can circulate to other lymphoid tissues but cannot recirculate.

L10 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2002 ACS
1976:15580 Document No. 84:15580 Control of immune response. I. Depression of DNA synthesis by immune lymph node cells. Asherson, G. L.; Wood, P. J.; Mayhew, Barbara (Div. Immunol., Clin. Res. Cent., Harrow, Engl.). Immunology, 29(6), 1057-65 (English) 1975. CODEN: IMMUAM.
AB After immunization of mice with picryl chloride the DNA response in the regional lymph nodes draining the site of immunization reached a peak on day 3 after immunization and fell to preimmunization levels by day 6. Prior i.v. **injection** with 40 .times. 106 immune lymph node cells depressed the day 4 DNA response by .apprx.60% but **injection** with 0.3 .times. 106 cells increased the DNA response. Similar results were obtained with another contact sensitizing agent, oxazolone, but cells immunized with oxazolone did not affect the DNA response to picryl chloride.

```
=> s l1 and syringe
L11           0 L1 AND SYRINGE

=> s l1 and dual chambered syringe
L12           0 L1 AND DUAL CHAMBERED SYRINGE

=> s (kundig t?/au or mccornmack s?/au)
L13         271 (KUNDIG T?/AU OR MCCORNMACK S?/AU)

=> s l13 and bee venom
L14           0 L13 AND BEE VENOM

=> s l13 and lymph node
L15          37 L13 AND LYMPH NODE

=> s l15 and injection
L16           7 L15 AND INJECTION

=> dup remove l16
PROCESSING COMPLETED FOR L16
L17           3 DUP REMOVE L16 (4 DUPLICATES REMOVED)

=> d l17 1-3 cbib abs

L17 ANSWER 1 OF 3     MEDLINE                          DUPLICATE 1
2002007199 Document Number: 21145839.    PubMed ID: 11248073.   Intralymphatic
```

immunization enhances DNA vaccination. Maloy K J; Erdmann I; Basch V; Sierro S; Kramps T A; Zinkernagel R M; Oehen S; **Kundig T M.** (Department of Dermatology, and Institute of Experimental Immunology, Universitatsspital Zurich, Schmelzbergstrasse 12, CH-8091 Zurich, Switzerland.. kevin.maloy@path.ox.ac.uk) . PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 Mar 13) 98 (6) 3299-303. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Although DNA vaccines have been shown to elicit potent immune responses in animal models, initial clinical trials in humans have been disappointing, highlighting a need to optimize their immunogenicity. Naked DNA vaccines are usually administered either i.m. or intradermally. The current study shows that immunization with naked DNA by direct **injection** into a peripheral **lymph node** enhances immunogenicity by 100- to 1,000-fold, inducing strong and biologically relevant CD8(+) cytotoxic T lymphocyte responses. Because **injection** directly into a **lymph node** is a rapid and easy procedure in humans, these results have important clinical implications for DNA vaccination.

L17 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS

1999:64705 Document No. 130:138281 A method of inducing a CTL response. **Kundig, Thomas M.**; Simard, John J. L. (CTL Immunotherapies Corporation, Can.). PCT Int. Appl. WO 9902183 A2 19990121, 199 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US14289 19980710. PRIORITY: CA 1997-2209815 19970710; US 1997-988320 19971210.

AB A method of inducing a cytotoxic T-lymphocyte (CTL) response to an antigen is disclosed. The method involves delivering the antigen to the lymphatic system of an animal regularly over a sustained period of time using, e.g., an osmotic pump. The method is advantageous over prior art methods for inducing a CTL response in that it does not require repetitive immunizations or the use of adjuvants. The method of the present invention can be used for the induction of CTLs in tumor or infectious disease immunotherapy.

L17 ANSWER 3 OF 3 MEDLINE

96281899 Document Number: 96281899. PubMed ID: 8676068. Induction of unresponsiveness and impaired T cell expansion by staphylococcal enterotoxin B in CD28-deficient mice. Mittrucker H W; Shahinian A; Bouchard D; **Kundig T M**; Mak T W. (Department of Immunology and Biophysics, Ontario Cancer Institute, University of Toronto, Ontario, Canada.) JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Jun 1) 183 (6) 2481-8. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB We used CD28-deficient mice to analyze the importance of CD28 costimulation for the response against Staphylococcal enterotoxin B (SEB) in vivo. CD28 was necessary for the strong expansion of V beta 8+ T cells, but not for deletion. The lack of expansion was not due to a failure of SEB to activate V beta 8+ T cells, as V beta 8+ T cells from both CD28-/- and CD28+/+ mice showed similar phenotypic changes within the first 24 h after SEB **injection** and cell cycle analysis showed that an equal percentage of V beta 8+ T cells started to proliferate. However, the phenotype and the state of proliferation of V beta 8+ T cells was different at later time points. Furthermore, in CD28-/- mice **injection** with SEB led to rapid induction of unresponsiveness in SEB responsive T cells, indicated by a drastic reduction of proliferation

after secondary SEB stimulation in vitro. Unresponsiveness could also be demonstrated in vivo, as CD28-/- mice produced only marginal amounts of TNF alpha after rechallenge with SEB. In addition CD28-/- mice were protected against a lethal toxic shock induced by a second **injection** with SEB. Our results indicate that CD28 costimulation is crucial for the T cell-mediated toxicity of SEB and demonstrate that T cell stimulation in the absence of CD28 costimulation induces unresponsiveness in vivo.

=> d his

(FILE 'HOME' ENTERED AT 11:57:15 ON 02 JUL 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 11:57:43 ON 02 JUL 2002

```
L1          104 S LYMPH NODE IMMUNIZATION
L2            1 S L1 AND ALLERGY
L3            0 S L1 AND AXILLARY LYMPH NODE
L4            4 S L1 AND INGUINAL
L5            1 DUP REMOVE L4 (3 DUPLICATES REMOVED)
L6            0 S L1 AND BEE VENOM
L7            0 S L1 AND ALLERGEN
L8            0 S L1 AND RADIOLOGICAL METHOD
L9           16 S L1 AND INJECTION
L10          10 DUP REMOVE L9 (6 DUPLICATES REMOVED)
L11           0 S L1 AND SYRINGE
L12           0 S L1 AND DUAL CHAMBERED SYRINGE
L13         271 S (KUNDIG T?/AU OR MCCORNMACK S?/AU)
L14           0 S L13 AND BEE VENOM
L15          37 S L13 AND LYMPH NODE
L16           7 S L15 AND INJECTION
L17           3 DUP REMOVE L16 (4 DUPLICATES REMOVED)

=> dup remove l15
PROCESSING COMPLETED FOR L15
L18          20 DUP REMOVE L15 (17 DUPLICATES REMOVED)

=> d l18 1-20 cbib abs

L18  ANSWER 1 OF 20  CAPLUS  COPYRIGHT 2002 ACS
2002:270882  Modulation of allergic response. Kundig, Thomas M.;
     McCormack, Stephen J. (Allecure Corporation, USA; University of Zurich).
     PCT Int. Appl. WO 2002028429 A2 20020411  DESIGNATED STATES: W:  AE, AG,
     AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ,
     DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,
     IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK,
     MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
     TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
     RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI,
     FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.
     (English).  CODEN: PIXXD2.  APPLICATION: WO 2001-US31088 20011005.
     PRIORITY: US 2000-PV237724 20001005; US 2001-804464 20010313.
AB   The modulation or elimination of an allergic condition according to the
     invention can be achieved by injecting small amts. of allergen directly
     into a lymph node, which greatly reduces the potential
     for side effects.

L18  ANSWER 2 OF 20  CAPLUS  COPYRIGHT 2002 ACS
2002:52003  Document No. 136:117371  Method of inducing an immunological CTL
     response by lymphatic system delivery of peptide vaccine. Kundig,
     Thomas M.; Simard, John J. L. (Switz.).  U.S. Pat. Appl. Publ. US
     20020007173 A1 20020117, 48 pp., Cont.-in-part of U. S. Ser. No. 380,534.
```

(English). CODEN: USXXCO. APPLICATION: US 2001-776232 20010202. PRIORITY: CA 1997-2209815 19970710; US 1997-988320 19971210; WO 1998-US14289 19980710; US 1999-380534 19990901.

AB Disclosed herein are methods for inducing an immunol. CTL response to an antigen by sustained, regular delivery of the antigen to a mammal so that the antigen reaches the lymphatic system. Antigen is delivered at a level sufficient to induce an immunol. CTL response in a mammal and the level of the antigen in the mammal's lymphatic system is maintained over time sufficient to maintain the immunol. CTL response. Also disclosed is an article of manuf. for delivering an antigen that induces a CTL response in an animal. The antigen can be used in vaccines for cancer or infection.

L18 ANSWER 3 OF 20 MEDLINE DUPLICATE 1

2002128163 Document Number: 21848226. PubMed ID: 11859099. Fucosyltransferase VII-deficient mice with defective E-, P-, and L-selectin ligands show impaired CD4+ and CD8+ T cell migration into the skin, but normal extravasation into visceral organs. Erdmann Iris; Scheidegger E Paul; Koch Frauke K; Heinzerling Lucie; Odermatt Bernhard; Burg Gunter; Lowe John B; **Kundig Thomas M.** (Department of Dermatology, University Hospital of Zurich, Gloriastrasse 31, 8091 Zurich, Switzerland.) JOURNAL OF IMMUNOLOGY, (2002 Mar 1) 168 (5) 2139-46. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The first step of leukocyte extravasation, leukocyte rolling, is mediated by E-, P-, and L-selectins. Mice deficient for alpha-1,3-fucosyltransferase VII (FucTVII)(-/-) are characterized by deficiency of E-, P-, and L-selectin ligand activity. This model system was used to evaluate the role of the interactions of selectins with their ligands in T and B cell responses. In the present study, FucTVII(-/-) mice showed reduced CD4+ T cell-mediated contact hypersensitivity reactions of the ears to FITC as well as reduced CD8+ T cell-mediated delayed-type hypersensitivity reactions of the footpads against lymphocytic choriomeningitis virus infection. As Langerhans cell migration to local **lymph nodes** as well as CD4+ and CD8+ T cell induction were found to be normal, the afferent arm of these reactions was not impaired. The reduced inflammatory reactions of the skin were due to inefficient lymphocyte extravasation into the skin. In contrast, extravasation of CD4+ and CD8+ T cells into visceral organs, such as the ovaries or the brain, was not impaired in FucTVII(-/-) mice. Elimination of vaccinia virus and of lymphocytic choriomeningitis virus from ovaries and brain, as well as elimination of tumor cells from several visceral organs was normal. Thus, interactions of selectins with their ligands are important for lymphocyte homing into the skin, but not for lymphocyte extravasation into visceral organs.

L18 ANSWER 4 OF 20 MEDLINE DUPLICATE 2

2002007199 Document Number: 21145839. PubMed ID: 11248073. Intralymphatic immunization enhances DNA vaccination. Maloy K J; Erdmann I; Basch V; Sierro S; Kramps T A; Zinkernagel R M; Oehen S; **Kundig T M.** (Department of Dermatology, and Institute of Experimental Immunology, Universitatsspital Zurich, Schmelzbergstrasse 12, CH-8091 Zurich, Switzerland.. kevin.maloy@path.ox.ac.uk) . PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 Mar 13) 98 (6) 3299-303. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB Although DNA vaccines have been shown to elicit potent immune responses in animal models, initial clinical trials in humans have been disappointing, highlighting a need to optimize their immunogenicity. Naked DNA vaccines are usually administered either i.m. or intradermally. The current study shows that immunization with naked DNA by direct injection into a peripheral **lymph node** enhances immunogenicity by 100- to 1,000-fold, inducing strong and biologically relevant CD8(+) cytotoxic T lymphocyte responses. Because injection directly into a **lymph**

node is a rapid and easy procedure in humans, these results have important clinical implications for DNA vaccination.

L18 ANSWER 5 OF 20 SCISEARCH COPYRIGHT 2002 ISI (R)
2001:969299 The Genuine Article (R) Number: 491UC. A novel method for continuous delivery of malignant melanoma vaccination peptides into superficial inguinal **lymph nodes**. Hauser M (Reprint); **Kundig T M**. RADIOLOGY (NOV 2001) Vol. 221, Supp. [S], pp. 293-294. Publisher: RADIOLOGICAL SOC NORTH AMERICA. 820 JORIE BLVD, OAK BROOK, IL 60523 USA. ISSN: 0033-8419. Language: English.

L18 ANSWER 6 OF 20 MEDLINE
2000488227 Document Number: 20492220. PubMed ID: 11037620. [Methods for increasing the immunogenicity of vaccines]. Verfahren zur Steigerung der Immunogenitat von Impfstoffen. **Kundig T M**. (Dermatologische Klinik, UniversitatsSpital Zurich.. tkuendig@derm.unizh.ch) . SCHWEIZERISCHE RUNDSCHAU FUR MEDIZIN PRAXIS, (2000 Sep 14) 89 (37) 1477-84. Journal code: 8403202. ISSN: 1013-2058. Pub. country: Switzerland. Language: German.
AB In the past years, enormous efforts have been undertaken to develop vaccine strategies against cancer. The aim is to have the immune system generate what are called killer cells that can specifically recognize the tumor. The surface of tumor cells contains MHC/HLA antigens which present short-chain peptides of tumor specific antigens. A large number of these oligopeptide antigens have been characterized in recent years. They are now available for use as tumor-specific vaccines. The problem is, however, that the immune response of producing T killer cells is very inefficient when these oligopeptide antigens are injected. As the physiological function of these killer cells virus-infected cells, a process associated with substantial tissue damage, the immune system has learned to use these killer cells with reticence over the course of evolution, in other words, when the life of the host is threatened. This does not happen until pathogens start to spread via lymphogenous or hematogenous pathways. And then it takes a certain amount of time after the invader is present for replication to take place. Since the oligopeptide antigens used as vaccines have a very short half-life in the tissue, not enough of them get to the **lymph nodes** and stay there for enough time to efficiently induce an immune response. Using a mouse model, we were able to show that the efficiency of the vaccine can be increased a million-fold by directly injecting the vaccine into a **lymph node** or the spleen which imitates lymphogenous or hematogenous spread. The efficiency of the "inactivated vaccine" can be enhanced even more by continuous administration of the vaccine over several days, simulating an especially dangerous virus replication. The evidence gathered in this mouse model was transferred to a clinical trial. The melanoma-specific inactivated vaccine is infused directly into a **lymph node** of tumor patients. The infusion is continued for several days. Booster vaccines are given every two weeks.

L18 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2002 ACS
1999:64705 Document No. 130:138281 A method of inducing a CTL response. **Kundig, Thomas M.**; Simard, John J. L. (CTL Immunotherapies Corporation, Can.). PCT Int. Appl. WO 9902183 A2 19990121, 199 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US14289 19980710. PRIORITY: CA 1997-2209815 19970710; US 1997-988320 19971210.
AB A method of inducing a cytotoxic T-lymphocyte (CTL) response to an antigen

is disclosed. The method involves delivering the antigen to the lymphatic system of an animal regularly over a sustained period of time using, e.g., an osmotic pump. The method is advantageous over prior art methods for inducing a CTL response in that it does not require repetitive immunizations or the use of adjuvants. The method of the present invention can be used for the induction of CTLs in tumor or infectious disease immunotherapy.

L18 ANSWER 8 OF 20 MEDLINE DUPLICATE 3
97240753 Document Number: 97240753. PubMed ID: 9120266. T cell development in mice expressing splice variants of the protein tyrosine phosphatase CD45. Kozieradzki I; **Kundig T**; Kishihara K; Ong C J; Chiu D; Wallace V A; Kawai K; Timms E; Ionescu J; Ohashi P; Marth J D; Mak T W; Penninger J M. (Department of Medical Biophysics, University of Toronto, Ontario, Canada.) JOURNAL OF IMMUNOLOGY, (1997 Apr 1) 158 (7) 3130-9. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB The transmembrane protein tyrosine phosphatase CD45 is expressed in multiple isoforms as a result of alternative splicing of variable exons encoding the extracellular domain. CD45 expression is critical for T cell development, and thymocyte maturation is blocked at the immature CD4+ CD8+ double-positive stage in CD45 gene-deficient (CD45 -/-) mice. Moreover, splicing of variable CD45 exons changes during thymocyte selection. To test the role of CD45 extracellular splice variants in T cell selection and development, we introduced CD45RO (a low-m.w. splice variant lacking exons 4, 5, and 6) and CD45ABC (a high-m.w. isoform containing all exons) transgenes under the control of a thymocyte-specific promoter into a CD45 -/- background, generating CD45RO transgene-positive CD45 -/- (CD45RO) and CD45ABC transgene-positive CD45 -/- (CD45ABC) mice. We demonstrate that both CD45 splice isoforms can rescue development of CD4+ and CD8+ TCR-alphabeta+ thymocytes. Neither CD45 isoform rescued positive selection of H-Y TCR transgene thymocytes, and these cells were blocked at a HSA(high) CD69- CD5(low) stage of development. Peripheral T cells from CD45RO and CD45ABC mice proliferated in response to allogeneic stimulator cells and anti-CD3epsilon cross-linking. However, only CD45RO mice, not CD45ABC mice, generated cytotoxic T cell responses and neutralizing, Th cell-dependent IgG Abs after viral infections. In addition, we show that T cells from CD45RO and CD45ABC mice accumulate in **lymph nodes** but not in the spleen, liver, or skin, indicating that the CD45 phosphatase may control the homing behavior and trafficking of T cells.

L18 ANSWER 9 OF 20 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
1997:132498 Document No.: PREV199799424311. Requirement for the transcription factor LSIRF/IRF4 for mature B and T lymphocyte function. Mittrucker, Hans-Willi; Matsuyama, Toshifumi; Grossman, Alex; **Kundig, Thomas M.**; Potter, Julia; Shahinian, Arda; Wakeham, Andrew; Patterson, Bruce; Ohashi, Pamela S.; Mak, Tak W. (1). (1) Dep. Med. Biophys., Univ. Toronto, 610 University Ave., Toronto, ON M5G 2C1 Canada. Science (Washington D C), (1997) Vol. 275, No. 5299, pp. 540-543. ISSN: 0036-8075. Language: English.

AB Lymphocyte-specific interferon regulatory factor (LSIRF) (now called IRF4) is a transcription factor expressed only in lymphocytes. Mice deficient in IRF4 showed normal distribution of B and T lymphocytes at 4 to 5 weeks of age but developed progressive generalized lymphadenopathy. IRF4-deficient mice exhibited a profound reduction in serum immunoglobulin concentrations and did not mount detectable antibody responses. T lymphocyte function was also impaired in vivo; these mice could not generate cytotoxic or antitumor responses. Thus, IRF4 is essential for the function and homeostasis of both mature B and mature T lymphocytes.

L18 ANSWER 10 OF 20 MEDLINE DUPLICATE 5

97404767 Document Number: 97404767. PubMed ID: 9261475. Expression of intercellular adhesion molecule 3 (CDw50) on endothelial cells in cutaneous lymphomas. A comparative study between nodal and cutaneous lymphomas. Dommann S N; Dommann-Scherrer C C; Ziegler T; Meyer J; Trueb R M; **Kundig T**; Panizzon R; Burg G. (Department of Dermatology, University Hospital of Zurich, Switzerland.) AMERICAN JOURNAL OF DERMATOPATHOLOGY, (1997 Aug) 19 (4) 391-5. Journal code: 7911005. ISSN: 0193-1091. Pub. country: United States. Language: English.

AB Advances in the molecular definition of surface proteins (adhesion molecules) involved in tumor metastasis may help to explain the invasive behavior of malignant tumors, that is, the migration of tumor cells involving reversible adhesive contacts, their release in the circulation, and their extravasation into distant sites. Intercellular adhesion molecule-3 (ICAM-3), the third receptor for the lymphocyte function-associated antigen molecule-1 (LFA-1) was recently characterized. We investigated fresh frozen skin biopsies from 10 patients with mycosis fungoides, four with pleomorphic T-cell lymphoma, six with Sezary syndrome, 10 with primary cutaneous B-cell lymphoma, and 10 with eczematous lesions as controls. The biopsies were compared with **lymph node** biopsies of five patients with known cutaneous T-cell lymphoma (CTCL), 10 with primary nodal B-cell lymphoma, and 11 with **lymph-node** specimens showing dermatopathic lymphadenopathy as controls. The specimens were stained with ICAM-3 antibody (Bender Medical Science) using the alkaline phosphatase antialkaline phosphatase method. Using cytomorphologic criteria, neoplastic lymphocytes could be differentiated from smaller reactive cells. Staining intensities were classified semiquantitatively as follows: 4, strong expression in 75 to 100% of the tumor cells; 3, 50 to 75%; 2, 25 to 50%; 1, 5 to 25%; and 0 fewer than 5% of the tumor cells. The endothelial cells in skin biopsies of seven of 30 primary cutaneous lymphomas expressed ICAM-3. In contrast, no expression of ICAM-3 could be demonstrated on endothelial cells in **lymph nodes** infiltrated with tumor cells of CTCL. Finally, endothelial cells of **lymph nodes** infiltrated with primary nodal B-cell lymphomas showed expression of ICAM-3 in three of 10 patients. The endothelial cells in the 11 control patients presenting with both eczematous lesions and dermatopathic lymphadenopathy showed no staining for ICAM-3. Every patient who expressed ICAM-3 on endothelial cells showed systemic spread of this disease. The findings suggest that ICAM-3 expression may be induced on endothelial cells in late-stage cutaneous lymphomas, probably by a cytokine-mediated mechanism.

L18 ANSWER 11 OF 20 MEDLINE DUPLICATE 6

97319821 Document Number: 97319821. PubMed ID: 9176709. Antigen localisation regulates immune responses in a dose- and time-dependent fashion: a geographical view of immune reactivity. Zinkernagel R M; Ehl S; Aichele P; Oehen S; **Kundig T**; Hengartner H. (Department of Pathology, University Hospital, Zurich, Switzerland.) IMMUNOLOGICAL REVIEWS, (1997 Apr) 156 199-209. Ref: 84. Journal code: 7702118. ISSN: 0105-2896. Pub. country: Denmark. Language: English.

AB This review summarises experimental evidence to illustrate that induction of immune reactivity depends upon antigen reaching and being available in lymphoid organs in a dose- and time-dependent manner. If antigen reaches lymph organs in a localised staggered manner and with a concentration gradient, a response is induced in the draining **lymph node**. Antigen-presenting cells are of critical importance to transport antigen from the periphery to local organised lymphoid tissue. If antigen is all over the lymphoid system, then it deletes all specific cells in the thymus or induces them within a few days; because of their limited life-span they then die off, leaving the repertoire depleted of this specificity. If antigen does not reach lymphoid organs it is ignored by immune cells. Once a response is induced, activated but not resting T cells will reach antigen outside lymphoid organs, whereas activated B

cells differentiate into plasma cells in an inducing environment, mostly in lymphoid tissue including bone marrow, but also in chronic lymphoid-like infiltrations in peripheral organs. In immunopathology (when the infectious agent is known) or in autoimmunity (when the triggering infectious agent is not known or not recognised) lymphoid tissue may become organised close to the antigen (e.g. in organ-specific autoimmune diseases) and may thereby maintain an autoantigen-driven disease-causing immune response for a long time. The notion that native T cells get induced or silenced in the periphery may be questioned because induction can only occur in lymphoid organs providing anatomical structures where critical cell-cell interactions are properly guided and where, therefore, cells are likely to meet sufficiently frequently and in a critical milieu. Since overall immune reactivity critically depends upon the localisation of antigens in a dose- and time-dependent manner, it seems more likely-but this remains to be shown-that activated T cells may get exhausted in non-lymphoid peripheral tissues, whereas they are usually maintained in lymphoid organs. The critical role of antigen in regulating immune responses also has relevance for our understanding of immunological defence against epithelial and mesenchymal tumours, against many infectious diseases and for understanding autoimmunity and immunological memory. Collectively the data indicate that antigen, dependent upon localisation, dose and time, seems to be the simplest regulator of immune responses.

L18 ANSWER 12 OF 20 MEDLINE

96281899 Document Number: 96281899. PubMed ID: 8676068. Induction of unresponsiveness and impaired T cell expansion by staphylococcal enterotoxin B in CD28-deficient mice. Mittrucker H W; Shahinian A; Bouchard D; **Kundig T M**; Mak T W. (Department of Immunology and Biophysics, Ontario Cancer Institute, University of Toronto, Ontario, Canada.) JOURNAL OF EXPERIMENTAL MEDICINE, (1996 Jun 1) 183 (6) 2481-8. Journal code: 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB We used CD28-deficient mice to analyze the importance of CD28 costimulation for the response against Staphylococcal enterotoxin B (SEB) in vivo. CD28 was necessary for the strong expansion of V beta 8+ T cells, but not for deletion. The lack of expansion was not due to a failure of SEB to activate V beta 8+ T cells, as V beta 8+ T cells from both CD28-/- and CD28+/+ mice showed similar phenotypic changes within the first 24 h after SEB injection and cell cycle analysis showed that an equal percentage of V beta 8+ T cells started to proliferate. However, the phenotype and the state of proliferation of V beta 8+ T cells was different at later time points. Furthermore, in CD28-/- mice injection with SEB led to rapid induction of unresponsiveness in SEB responsive T cells, indicated by a drastic reduction of proliferation after secondary SEB stimulation in vitro. Unresponsiveness could also be demonstrated in vivo, as CD28-/- mice produced only marginal amounts of TNF alpha after rechallenge with SEB. In addition CD28-/- mice were protected against a lethal toxic shock induced by a second injection with SEB. Our results indicate that CD28 costimulation is crucial for the T cell-mediated toxicity of SEB and demonstrate that T cell stimulation in the absence of CD28 costimulation induces unresponsiveness in vivo.

L18 ANSWER 13 OF 20 MEDLINE

96178468 Document Number: 96178468. PubMed ID: 8598042. Impaired negative selection of T cells in Hodgkin's disease antigen CD30-deficient mice. Amakawa R; Hakem A; **Kundig T M**; Matsuyama T; Simard J J; Timms E; Wakeham A; Mittruecker H W; Griesser H; Takimoto H; Schmits R; Shahinian A; Ohashi P; Penninger J M; Mak T W. (Amgen Institute, Department of Medical Biophysics, University of Toronto, Ontario, Canada.) CELL, (1996 Feb 23) 84 (4) 551-62. Journal code: 0413066. ISSN: 0092-8674. Pub. country: United States. Language: English.

AB CD30 is found on Reed-Sternberg cells of Hodgkin's disease and on a

variety of non-Hodgkin's lymphoma cells and is up-regulated on cells after Epstein-Barr virus, human T cell leukemia virus, and HIV infections. We report here that the thymus in CD30-deficient mice contains elevated numbers of thymocytes. Activation-induced death of thymocytes after CD3 cross-linking is impaired both in vitro and in vivo. Breeding the CD30 mutation separately into alpha beta TCR-or gamma delta TCR-transgenic mice revealed a gross defect in negative but not positive selection. Thus, like TNF-receptors and Fas/Apo-1, the CD30 receptor is involved in cell death signaling. It is also an important coreceptor that participates in thymic deletion.

L18 ANSWER 14 OF 20 MEDLINE

96376850 Document Number: 96376850. PubMed ID: 8782702. On T cell memory: arguments for antigen dependence. **Kundig T M**; Bachmann M F; Ohashi P S; Pircher H; Hengartner H; Zinkernagel R M. (Institute for Experimental Immunology, Zurich.) IMMUNOLOGICAL REVIEWS, (1996 Apr) 150 63-90. Ref: 100. Journal code: 7702118. ISSN: 0105-2896. Pub. country: Denmark. Language: English.

AB Memory is a hallmark of the immune system. Considerable progress has been made towards understanding B cell memory, but T cell memory remains poorly understood and its nature is controversial. There is good evidence that B cell memory is driven by antigen, but the antigen dependence of T cell memory is still being debated. For several years we have investigated the nature, duration and antigen dependence of different aspects of CD8+ T cell memory and this review will discuss our findings as well as how and why they differ from some other results. As others, we find that antigen, due to proliferation of antigen-specific T cell clones, induces a shift in the T cell repertoire which remains detectable for years as an elevated cytotoxic T cell precursor frequency (CTLp) in lymphoid organs. Also in the absence of antigen, in vitro assays for T cell memory which invariably isolate memory T cells from these lymphoid organs therefore remain positive. In contrast, immunity against reinfection with a pathogen requires more than just elevated numbers of CTLp in lymphoid organs. Since reinfection usually takes place via peripheral nonlymphoid tissue, these CTLp have to a) efficiently extravasate and patrol through such tissues, and b) be immediately able to exert effector function in case of reinfection. Both functions, require a certain level of activation which critically depends on T cell stimulation by persisting antigen.

L18 ANSWER 15 OF 20 MEDLINE

95288636 Document Number: 95288636. PubMed ID: 7770771. Deregulated T cell activation and autoimmunity in mice lacking interleukin-2 receptor beta. Suzuki H; **Kundig T M**; Furlonger C; Wakeham A; Timms E; Matsuyama T; Schmits R; Simard J J; Ohashi P S; Griesser H; +. (Amgen Institute, Toronto, Ontario, Canada.) SCIENCE, (1995 Jun 9) 268 (5216) 1472-6. Journal code: 0404511. ISSN: 0036-8075. Pub. country: United States. Language: English.

AB In mice lacking the interleukin-2 receptor beta chain (IL-2R beta), T cells were shown to be spontaneously activated, resulting in exhaustive differentiation of B cells into plasma cells and the appearance of high serum concentrations of immunoglobulins G1 and E as well as autoantibodies that cause hemolytic anemia. Marked infiltrative granulocytopoiesis was also apparent, and the animals died after about 12 weeks. Depletion of CD4+ T cells in mutant mice rescued B cells without reversion of granulocyte abnormalities. T cells did not proliferate in response to polyclonal activators, nor could antigen-specific immune responses be elicited. Thus, IL-2R beta is required to keep the activation programs of T cells under control, to maintain homeostasis, and to prevent autoimmunity.

L18 ANSWER 16 OF 20 MEDLINE DUPLICATE 7

95015826 Document Number: 95015826. PubMed ID: 7930564. Free recirculation of memory B cells versus antigen-dependent differentiation

to antibody-forming cells. Bachmann M F; **Kundig T M**; Odermatt B; Hengartner H; Zinkernagel R M. (Department of Pathology, University of Zurich, Switzerland.) JOURNAL OF IMMUNOLOGY, (1994 Oct 15) 153 (8) 3386-97. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB This study investigated whether or not the localization of persisting Ag influenced the localization of memory B and/or of Ab-forming cells (AFC). As a model Ag, we used vesicular stomatitis virus, which does not measurably replicate extraneuronally in adult mice after peripheral infection. Our results show that memory B cells and AFC are induced at the site where Ag is present; induced memory B cells then recirculate throughout the lymphoid system independently of Ag localization. In contrast, AFC are induced only at the sites of Ag persistence. These triggered Ab producing cells do not recirculate through the lymphoid tissue but migrate to the bone marrow.

L18 ANSWER 17 OF 20 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

94264260 EMBASE Document No.: 1994264260. Reduced thymic maturation but normal effector function of CD8+ T cells in CD8.beta. gene-targeted mice. Fung-Leung W.-P.; **Kundig T.M.**; Ngo K.; Panakos J.; De Sousa-Hitzler J.; Wang E.; Ohashi P.S.; Mak T.W.; Lau C.Y.. R. W. Johnson Pharmaceut. Res. Inst., 19 Green Belt Drive,Don Mills, Ont. M3C 1L9, Canada. Journal of Experimental Medicine 180/3 (959-967) 1994. ISSN: 0022-1007. CODEN: JEMEAV. Pub. Country: United States. Language: English. Summary Language: English.

AB CD8 is a cell surface glycoprotein on major histocompatibility complex class I-restricted T cells. Thymocytes and most peripheral T cells express CD8 as heterodimers of CD8.alpha. and CD8.beta.. The intestinal intraepithelial lymphocytes (IEL), which have been suggested to be generated extrathymically, express CD8 predominantly as homodimers of CD8.alpha.. We have generated CD8.beta. gene-targeted mice. CD8.alpha.+ T cell population in the thymus and in most peripheral lymphoid organs was reduced to 20-30% of that in wild-type littermates. CD8.alpha. expression on thymocytes and peripheral T cells also decreased to 44 and 53% of the normal levels, respectively. In contrast, neither the population size nor the CD8.alpha. expression level of CD8.alpha.+ IEL was reduced. This finding indicates that CD8.beta. is important only for thymic- derived CD8+ T cells. The lack of CD8.beta. reduces but does not completely abolish thymic maturation of CD8+ T cells. Our result also reveals the role of CD8.beta. in regulating CD8.alpha. expression on thymic derived T cells. Peripheral T cells in these mice were efficient in cytotoxic activity against lymphocytic choriomeningitis virus and vesicular stomatitis virus, suggesting that CD8.beta. is not essential for the effector function of CD8+ T cells.

L18 ANSWER 18 OF 20 MEDLINE

94112120 Document Number: 94112120. PubMed ID: 7904347. CD4 negative mice as a model for immunodeficiency. Rahemtulla A; Shahinian A; **Kundig T**; Zinkernagel R; Mak T W. (Amgen Institute, Toronto, Ontario, Canada.) PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY OF LONDON. SERIES B: BIOLOGICAL SCIENCES, (1993 Oct 29) 342 (1299) 57-8. Journal code: 7503623. ISSN: 0962-8436. Pub. country: ENGLAND: United Kingdom. Language: English.

AB CD4 is a co-receptor required for T cell helper functions. A mouse strain without CD4 expression has been generated. These animals, surprisingly have a normal CTL response and reduced, but not absent, humoral responses. A new population of MHC class II restricted CD4-CD8-TcR alpha beta+ T cells has emerged which possess helper function potential. These findings have important implications on disease situations where CD4 cells are decreased or absent.

L18 ANSWER 19 OF 20 MEDLINE

91208681 Document Number: 91208681. PubMed ID: 1673361. CD8 is needed for

development of cytotoxic T cells but not helper T cells. Fung-Leung W P; Schilham M W; Rahemtulla A; **Kundig T M**; Vollenweider M; Potter J; van Ewijk W; Mak T W. (Ontario Cancer Institute, University of Toronto, Canada.) CELL, (1991 May 3) 65 (3) 443-9. Journal code: 0413066. ISSN: 0092-8674. Pub. country: United States. Language: English.

AB A mutant mouse strain without CD8 (Lyt-2 and Lyt-3) expression on the cell surface has been generated by disrupting the Lyt-2 gene using embryonic stem cell technology. In these mice, CD8+ T lymphocytes are not present in peripheral lymphoid organs, but the CD4+ T lymphocyte population seems to be unaltered. Cytotoxic response of T lymphocytes from these mice against alloantigens and viral antigens is dramatically decreased. Proliferative response against alloantigens and in vivo help to B lymphocytes, however, are not affected. These data suggest that CD8 is necessary for the maturation and positive selection of class I MHC restricted cytotoxic T lymphocytes but is not required on any of the intermediate thymocyte populations (CD8+CD4-TcR- or CD4+CD8+TcRlow) during the development of functional class II MHC restricted helper T cells.

L18 ANSWER 20 OF 20 MEDLINE

91367264 Document Number: 91367264. PubMed ID: 1832488. Normal development and function of CD8+ cells but markedly decreased helper cell activity in mice lacking CD4. Rahemtulla A; Fung-Leung W P; Schilham M W; **Kundig T M**; Sambhara S R; Narendran A; Arabian A; Wakeham A; Paige C J; Zinkernagel R M; +. (Department of Medical Biophysics and Immunology, University of Toronto, Ontario, Canada.) NATURE, (1991 Sep 12) 353 (6340) 180-4. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB T cells express T-cell antigen receptors (TCR) for the recognition of antigen in conjunction with the products of the major histocompatibility complex. They also express two key surface coreceptors, CD4 and CD8, which are involved in the interaction with their ligands. As CD4 is expressed on the early haemopoietic progenitor as well as the early thymic precursor cells, a role for CD4 in haemopoiesis and T-cell development is implicated. Thymocytes undergo a series of differentiation and selection steps to become mature CD4+8- or CD4-8+ (single positive) T cells. Studies of the role of CD4+ T cells in vivo have been based on adoptive transfer of selected or depleted lymphocytes, or in vivo treatment of thymectomized mice with monoclonal antibodies causing depletion of CD4+ T cells. In order to study the role of the CD4 molecule in the development and function of lymphocytes, we have disrupted the CD4 gene in embryonic stem cells by homologous recombination. Germ-line transmission of the mutation produces mutant mouse strains that do not express CD4 on the cell surface. In these mice, the development of CD8+ T cells and myeloid components is unaltered, indicating that expression of CD4 on progenitor cells and CD4+ CD8+ (double positive) thymocytes is not obligatory. Here we report that these mice have markedly decreased helper cell activity for antibody responses, although cytotoxic T-cell activity against viruses is in the normal range. This differential requirement for CD4+ helper T cells is important to our understanding of immune disorders including AIDS, in which CD4+ cells are reduced or absent.

```
=> s l1 and phospholipase A2
L19           0 L1 AND PHOSPHOLIPASE A2

=> s l1 adn PLA2
MISSING OPERATOR L1 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l1 and "PLA2"
L20           0 L1 AND "PLA2"
```

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	100.64	100.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.58	-5.58